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Environmental Health Research Implications of Methylmercury

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In “Adverse Effects of Methylmercury: Environmental Health Research Implications,” Grandjean et al. (2010) reviewed the scientific discoveries of health risks resulting from methylmercury exposure, including the history of the Minamata disease incident. Although their title states “research implications,” the authors failed to convey some important caveats from the incident.

First, Grandjean et al. (2010) explained the incident as if serious delays of the recognition of “the exact cause (methylmercury)” deferred the corrective action. However, recognition of an etiologic agent is not a necessary condition for prevention (Goodman et al. 1990). When source and transmission are identified, they must be eliminated even if the etiologic agent is unknown. In the case of Minamata disease, even in 1956 when the first patient was identified, eating contaminated seafood was determined to be a cause of the disease; this occurred 3 years before the etiologic agent was identified (Tsuda et al. 2009). Grandjean et al. (2010) cited Harada (2004), who wrote,

However, with no specific causative substance [etiologic agent] determined, there was no legal basis for a ban on fishing. (Under Item 2 of the Food Sanitation Act, it was not possible to prohibit fishing while the cause was undetermined.)

However, in Japan, even with no specific etiologic agent determined, the Food Sanitation Act has routinely been enacted when causal food and/or causal facility was determined.

Second, Grandjean et al. (2010) mentioned the “diagnostic difficulties” of methylmercury poisoning cases. Lack of investigation of the Minamata disease incident as food poisoning resulted in unnecessary diagnostic difficulties; such difficulties do not usually arise in food-poisoning incidents in Japan. In the case of Minamata disease, in 1977 the Japanese Ministry of Environment (JME) established the criteria for diagnosis, which required combinations of signs that were advocated by the JME to be medically correct. However, the truth is that the JME recognized a lack of medical evidence on the criteria [Committee on Research and Human Rights/Japanese Society and Psychiatry and Neurology (CRHR-JSPN) 2003]. Moreover, medical researchers in Japan have pointed out that the criteria were medically incorrect (CRHR-JSPN 1998). The “diagnostic difficulties” may have obscured who was affected and had neurological signs.

Third, Grandjean et al. (2010) stated that, “Only in 2009 was a law enacted to provide compensation to most of the remaining group of victims.” However, it was not compensation. For Minamata disease, unless the affected persons are diagnosed by the above-mentioned criteria, they are not counted as patients and are thus not properly compensated. About 2,200 patients have been diagnosed with Minamata disease and have been compensated, whereas at least several tens of thousands of victims who have neurological signs characteristic of methylmercury poisoning have not been recognized as patients and have not been properly compensated (McCurry 2006).

Fourth, Grandjean et al. (2010) described the “scientific account” of the cat experiment in 1959, which was published after a 40-year delay (Eto et al. 2001). However, the report provided only pathological findings, and the detailed explanation of the cat experiment had already been published in 1965 (Tomita 1965). The latter would be enough for prevention and control.

Finally, because the JME and local governments have been defendants in Minamata disease lawsuits, research funds from JME and the local governments may affect researchers’ attitudes, possibly causing conflicts of interest.

T.T. and M.H. have provided expert testimony on Minamata disease. The other author declares he has no actual or potential competing financial interests.

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Methylmercury: Grandjean et al. Respond

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We thank Tsuda et al. for sharing their views. Along with their previous publications on Minamata disease, we find their comments useful as a complement to our brief historical review of the mass poisonings in Japan and associated events (Grandjean et al. 2010). However, the specific issues raised in their letter do not affect our conclusions on the research implications of the history of methylmercury science.

P.G. has provided paid expert testimony on mercury toxicology in a legal case concerning environmental pollution from coal-powered power plants. The other authors declare that they have no actual or potential competing financial interests.

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Particulate Matter–Induced Health Effects: Who Is Susceptible?

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We read with great interest a recent review by Sacks et al. (2011) and would like to add some comments to facilitating effects of particulate matter (PM) on preexisting respiratory diseases. First of all, the adverse effects of PM/diesel exhaust particles (DEP) on chronic obstructive pulmonary disease (COPD) pathophysiology seem to be controversial. Subjects with pulmonary emphysema are epidemiologically susceptible to PM (Dockery et al. 1993; Euler et al. 1987; MacNee and Donaldson 2003; Thishan Dharshana and Coowanitwong 2008). Further, as noted by Sacks et al. (2011), Lopes et al. (2009) have experimentally shown that chronic (2 months) exposure to an ambient level (mean concentration, $34 \mu\text{g}/\text{m}^3$) of PM_{10} ($\text{PM} < 10 \mu\text{m}$ in aerodynamic diameter) worsens murine emphysema induced by papain. In contrast, in our previous study (Inoue et al. 2010) we did not obtain apparent evidence that a single intratracheal administration of DEP [200 $\mu\text{g}/\text{animal}$, a dose high enough to worsen infectious lung injury (Takano et al. 2002)] exacerbates porcine pancreatic elastase–elicited pulmonary emphysema in mice. Possible explanations for this opposite phenomenon may include differences in animal strains or species, pathological conditions (type and/or degree of emphysematous inflammation), and/or DEP exposure protocols (route, dose, timing, duration, and/or terminal point). Additional in-depth studies will be required to conclude PM/DEP has adverse effects on COPD pathophysiology.

Secondly, from a biological point of view, pulmonary fibrosis (PF) should be

added to the list of PM-susceptible respiratory diseases. Recently, Decolonne et al. (2010) showed that exposure to carbon black nanoparticles exacerbates bleomycin-induced PF in mice. More recently, we demonstrated that a single intratracheal instillation of tiny carbon black nanoparticles (14 nm) at a dose of 10 $\mu\text{g}/\text{mouse}$ aggravates PF, suggesting that exposure to trace amounts of PM can exacerbate pathophysiology (Kamata et al. 2011). Accordingly, careful attention should be paid to PF patients who are at risk of environmental and occupational exposure to PM, although further basic and clinical research is necessary.

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Editor's note: In accordance with journal policy, Sacks et al. were asked whether they wanted to respond to this letter, but they chose not to do so.

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